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Antimicrobial Use in Positive Respiratory Viral Panel: Impact of Procalcitonin Use and Antimicrobial Stewardship

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Introduction

Antimicrobial stewardship is a systematic effort to avoid antibiotic overuse in response to increasing antibiotic resistant microbes.[1] Blood and sputum cultures are the gold standard for bacterial identification, but they are difficult to obtain and take days to receive back from the lab. Physicians commonly treat patients empirically with antibiotics because there is an increased risk of 30-day mortality in patients with bacterial community-acquired pneumonia (CAP).[2] Overuse of antibiotics is commonplace in hospitalized patients which is detrimental as it contributes to antibiotic resistance, costs money, wastes resources, and puts patients at risk for unnecessary adverse effects of the medications.[3] It was found that 75% of patients presenting with a respiratory tract infection receive antibiotics despite evidence of viral etiology.[4]

Various biomarkers have been used to try to distinguish between bacterial and viral infections, including procalcitonin (PCT) which is a peptide precursor of calcitonin. Evidence shows that PCT is undetectable in healthy individuals and increases in response to bacterial toxins and cytokines, but not to virally stimulated interferon-γ.[5] PCT's highly sensitive response to bacterial infections makes it superior to other inflammatory biomarkers such as C-reactive protein and erythrocyte sedimentation rate.[3,4]
PCT levels change in response to therapeutic treatment, increasing with bacterial infection and decreasing upon recovery, making them exceptional markers to monitor treatment.[6] Levels are measured upon admission and are taken serially throughout hospitalization.[3] PCT becomes measurable in the serum within 2-4 hours of inflammatory response to infection peaking after 12 hours.[4] PCT is a marker for systemic infection, as levels are normal or undetectable in healthy patients and patients with mild-to-moderate acute respiratory infection (ARI).[7] PCT levels were also associated with a higher mortality risk in severe infection.[6]

Being highly sensitive to bacterial infection and responsive to treatment, PCT can be used to determine when antibiotics should be prescribed or discontinued in respiratory illnesses.[4] Antibiotics were discouraged for PCT levels <0.25 ng/mL and encouraged for levels >0.25 ng/mL, while normal is <0.03 ng/mL.[8] Following these criteria, antibiotics were reduced by 72% without a change in patient morbidity, treatment failure, or mortality.[9]

The Miami Valley Hospital Antimicrobial Stewardship Team was formed in 2014 consisting of one pharmacist and one doctor for 40 hours per month. The aim of the program was to decrease the use of antibiotics to prevent resistant microbes from developing. This study began as a prospective audit of hospitalized patients on PCT guided therapy focusing on ICU patients, patients on broad spectrum antibiotics and patients on multiple antibiotics.

This quality improvement study aims to assess the use of PCT in patients diagnosed with viral respiratory infections. Our assessment focused on determining if using PCT-guided therapy effectively reduces antibiotic use without changing patient outcomes. We also evaluated whether PCT levels alter the course of antibiotic therapy for bacterial infections.

Research Questions

1. Has the Antimicrobial Stewardship Team been able to utilize PCT to decrease antibiotic stewardship use in patients with viral respiratory infections?

2. Does PCT-guided therapy improve outcomes (by decreasing cost and mortality) in hospitalized patients with diagnosed respiratory infections?

3. Do PCT levels appropriately alter antibiotic courses by maintaining patient outcomes (by decreasing cost and mortality) while decreasing antibiotic overuse?

Methodology

We reviewed all positive polymerase chain reaction (PCR) panels during flu season at Miami Valley Hospital (MVH). PCR panels are a sensitive test used to confirm viral etiology in infections. Flu season was defined as the months of November through April between 2015 and 2018. A preliminary review determined that 800 patients met these inclusion criteria. This was an adequate sample size because when the patients were stratified by year of admission each group's size was still greater than 30, which was the general sample size required for adequate observation.[10]

Our inclusion criteria were the following:

1. Positive respiratory virus PCR
2. Admitted to MVH for at least 1 midnight (MVH's determination of inpatient status)

These charts were reviewed focusing on PCT levels, chest x-ray, length of stay, and antibiotic duration. A PCT was considered elevated if above 0.5 ng/mL. Patient data was de-identified and did not leave MVH.

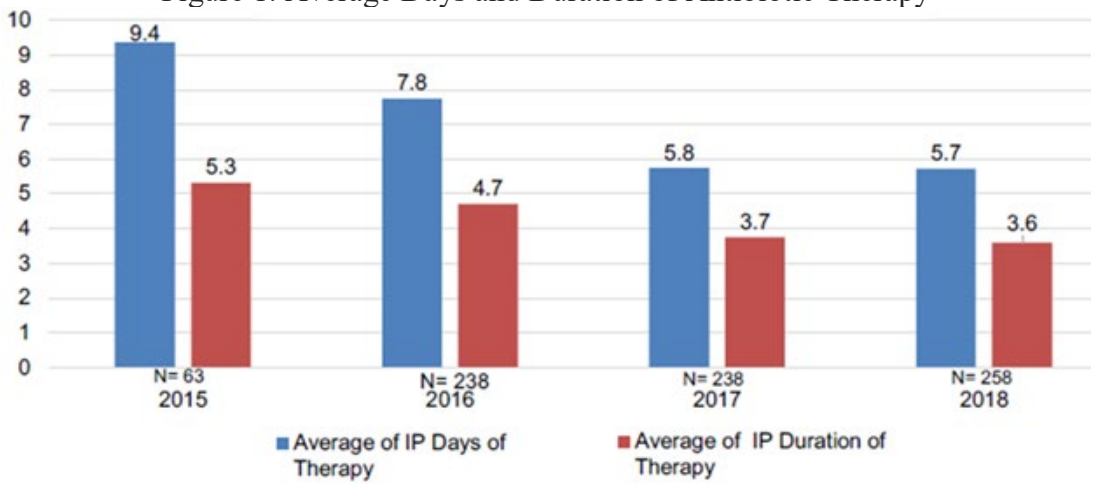
Data analysis

All results were analyzed using SPSS software. Independent sample T-tests determined if antibiotic use or hospital stay duration was decreased between 2015 and 2018. Independent T-tests were used to compare the mean number of days of antibiotic therapy between patients with an abnormal chest x-ray and a positive PCT versus patients with a normal chest x-ray and negative PCT. We determined if there is a significant difference in days of antibiotic therapy or length of stay between patients with an abnormal chest x-ray and a positive PCT and patients with a normal chest x-ray and negative PCT. This study design made sense because a patient with a positive PCT was likely to have a bacterial infection causing an abnormal chest x-ray. A patient with a negative PCT was more likely to have a normal chest x-ray. By comparing these two dichotomies we determined whether PCT guided therapy made a significant difference in treatment duration and patient mortality.

Results

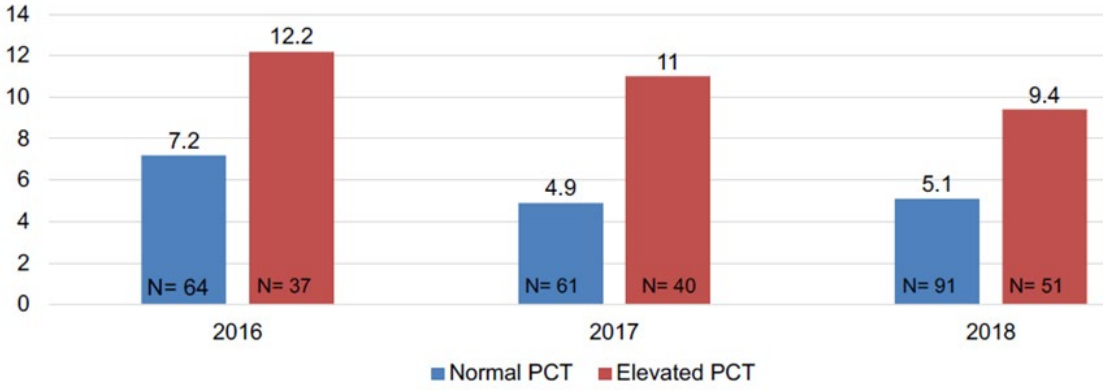
The initiation of PCT guided therapy correlated with a significant decrease in the average days of therapy from 9.4 to 5.7 days ($p = 0.003$). The average duration of therapy 5.3 to 3.6 days ($p = 0.004$) was also found to significantly decrease during this time (Figure 1).

Figure 1. Average Days and Duration of Antibiotic Therapy



Both patients with elevated and normal PCTs showed a significant decrease in the days of therapy and the duration of antibiotic use. Patients with elevated PCT were found to have significantly fewer days of therapy from 12.2 days to 9.4 days, whereas patients with a normal PCT decreased from 7.2 days to 5.1 days of therapy. Patients with an elevated PCT required more days and a longer duration of antibiotic therapy (Figure 2).

Figure 2. Average Days of Antibiotic Therapy based on PCT level



Patients with an abnormal chest x-ray and an elevated PCT received significantly more days of antibiotic therapy (11.2) compared to patients with a normal chest x-ray and normal PCT (4.6) (Figure 3, p = 0.002).

Figure 3. Average Days of Antibiotic Therapy based on PCT and CXR results

The length of hospital stay was not significantly changed during this time, 6.2 days in 2015 to 6 days in 2018 (p = 0.766).

Discussion

By utilizing PCT levels, the Antimicrobial Stewardship Team has been able to decrease antibiotic use in patients with viral respiratory infections. Both the days of antibiotics and duration of antibiotics were decreased. With earlier discontinuation of antibiotics, outcomes were not shown to be statistically different. The average length of stay remained around 6 day. Our data support that implementation of PCT, along with antibiotic stewardship, decreased antimicrobial use in patients with diagnosed viral infection.

Recent studies highlighted the ambiguity of the sensitivity and specificity of using PCT levels alone for prediction of bacterial infection and as a tool for antibiotic discontinuation. A recent meta-analysis found " a single procalcitonin level of 0.5 µg/mL … with an overall sensitivity of 55% for detecting bacterial infection,"[11] whereas other studies found "a cutoff value of ≥0.5 ng/ mL had a sensitivity of 73%–100%."[12] Based on our data, an elevated PCT and an abnormal chest x-ray were more likely to receive more

days and duration of antibiotic use. Likewise, a normal PCT and a normal x-ray were less likely to need as many days and duration of antibiotics. We found a significant decrease in antibiotic use when adding a chest x-ray result to a PCT suggesting that prescribers were more likely to discontinue antibiotic therapy with the two results together, than each result alone. Future studies should focus on whether PCT alone can be an effective driver of antibiotic discontinuation. As it is now, we believe PCT guided therapy is best utilized as a tool to help the physician in their clinical decision making but should not be used alone without other confirmatory studies.

Our study focused solely on patients who had a positive respiratory virus PCR who were admitted to MVH greater than 1 midnight during flu season between 2015 and 2018. It was limited to the context of respiratory viral illnesses as this was the focus population of our study. Although most patients with renal dysfunction will have a normal PCT, levels can be increased in patients with renal dysfunction due to decreased clearance.[13] Our heterogeneous population included patients with renal disease which may have contributed to falsely elevated PCT levels. This was another reason we believe PCT levels should be used in the greater context of patient care and not as the sole determiner of antibiotic use.

Conclusion

After the implementation of antimicrobial stewardship (ASP) in 2014 and increased utilization of PCT-guided therapy in 2016, Miami Valley Hospital effectively decreased antibiotic use in patients with confirmed respiratory viral infections without any negative effects on length of stay. While the use of PCT alone for determination of antibiotic discontinuation remains a topic of contention, use in conjunction with imaging and clinical presentation has been shown to be effective in the local context of MVH.

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